SCREENING FOR VIRAL HEPATITIS DURING THE REFUGEE DOMESTIC NEW ARRIVAL MEDICAL EXAMINATION

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I. Introduction

Viral hepatitis is the presence of inflammatory cells in the liver due to hepatocyte infection with a hepatotropic virus. Infection can be characterized as acute (less than 6 months) or chronic (6 months or longer). Although multiple viruses may cause both acute and chronic hepatitis, this document will address the hepatotropic viral etiologies that account for an overwhelming majority of infectious hepatitides: hepatitis A, B, C, D and E viruses. The leading infectious causes of acute hepatitis are hepatitis viruses A and E, which account for more than 95% of viral hepatitides worldwide. The most common viral etiologies of chronic hepatitis are hepatitis B virus (HBV), followed by hepatitis C virus (HCV). Hepatitis B and C virus infections are associated with the development of cirrhosis and hepatocellular carcinoma (HCC). Hepatitis D virus (HDV) infection, caused by hepatitis delta agent, can propagate only in the presence of hepatitis B virus. HBV/HDV co-infection leads to more severe liver disease than HBV mono-infection and is associated with increased risk of development of HCC.

II. Summary of Recommendations

This section provides a summary of recommendations for serologic screening for viral hepatitis in asymptomatic refugees during the new arrival domestic medical examination for refugees. More detailed discussion is provided in subsequent sections of this document.

Chronic Viral Hepatitis

Hepatitis B

Adults

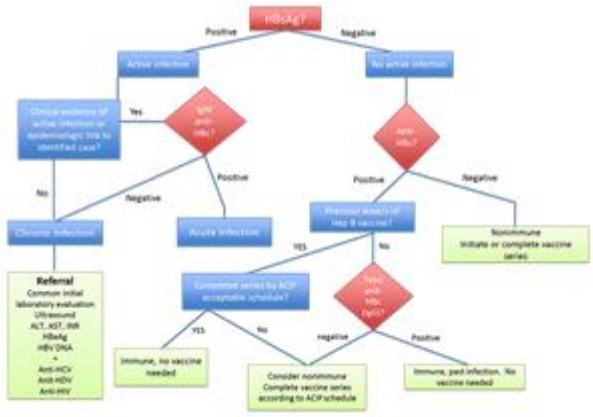

Figure 1. Hepatitis B screening algorithm for those ≥ 18 years born in countries with hepatitis B prevalence rates of ≥ 2%, or those considered at risk in countries where prevalence rates are < 2%.

- All adults >18 years of age who were born in or most recently lived in countries where the rate of chronic hepatitis B virus infection is >2% (intermediate or highly endemic countries) should be tested for hepatitis B surface antigen (HBsAg), as well as antibodies to hepatitis B core antigen (anti-HBc) and hepatitis B surface antigen (anti-HBs) (Figure 1). Testing for HBsAg* should be performed regardless of vaccination history.**
- Most refugee groups currently resettling to the United States originate from or have lived in countries with intermediate or high endemnicity.
- All adults >18 years of age who have lived in countries where the rate of chronic hepatitis B virus infection is < 2% (low prevalence) should be tested for HBsAg and antibodies to

hepatitis B core antigen (anti-HBc) and hepatitis B surface antigen (anti-HBs)*** if they are in a high-risk group, including:

- Men who have sex with men
- Persons who currently use or have recently used injection drugs
- Persons who are from a low-prevalence country but are part of a subpopulation that has a known prevalence rate of > 2% (e.g., some indigenous populations)
- Persons receiving chronic hemodialysis
- HIV-infected persons
- Persons with chronic liver disease (e.g., HCV-infected persons)
- Heterosexual men and women with multiple sex partners or a history of sexually transmitted infections
- Persons with previous employment in health care or in care institutions for the developmentally disabled
- Persons who have received whole blood or blood components prior to migration
- Persons with a history of incarceration
- Persons with a history of potential exposure to reused or nonsterile invasive medical devices

- All adults living in households or close quarters with a chronically infected person should be tested for HBV infection and should receive the 3-dose hepatitis B vaccine series if susceptible.
- All pregnant women should receive HBsAg testing. Infants of HBsAg-positive mothers require hepatitis B immunization and hepatitis B immune globulin (HBIG) at birth.
- Any adult with potential exposure to hepatitis B virus within 60 days of the new arrival examination should have repeat testing 3-6 months after arrival.

Children <18 Years of Age

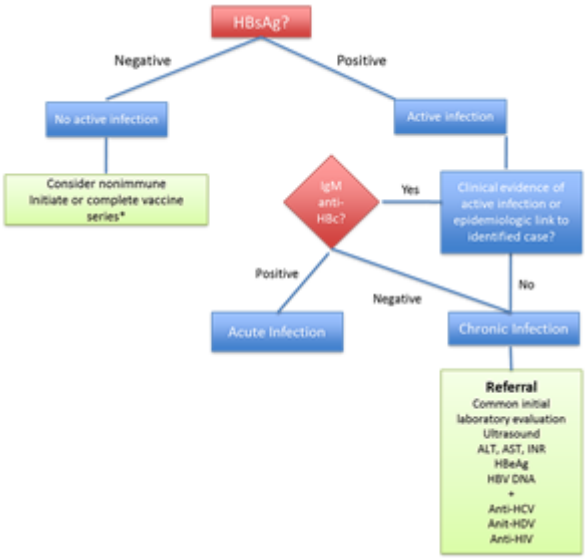

Figure 2. Hepatitis B screening algorithm for those < 18 years born in countries with hepatitis B prevalence rates of ≥ 2%.

- As for adults, all refugee children <18 years who were born in or have lived in countries where the rate of chronic HBV infection is >2% (intermediate or high-endemicity countries) should be tested for HBsAg. Screening for anti-HBc and anti-HBs is not routine but may be considered to determine past exposure and immune status, although screening in children may be less cost-effective (Figure 2). Testing for HBsAg* should be done regardless of vaccination history.**
- All refugee children who have resided in a country with a rate of < 2% (low endemnicity) should receive testing for hepatitis B surface antigen (HBsAg) if they have any risk factors for hepatitis B, including:
    - Infants born to HBsAg-positive mothers
    - Children with an immediate family member, particularly the biological mother, who is chronically infected with HBV
    - Children from a low-prevalence country who are part of a subpopulation that has a known prevalence rate of ≥2% (e.g., some indigenous populations)
    - HIV-infected children
    - Children who received whole blood or blood components prior to migration.
    - Children with a potential exposure to hepatitis B within 60 days of the new arrival examination should be tested again 3-6 months after arrival.
    - Children with a history of injection drug use (IDU) or who have multiple sex partners or have a history of sexual exploitation.
- All children ≤18 years old who are HBsAg negative should receive the complete hepatitis B vaccine series according to ACIP guidelines (www.cdc.gov/vaccines/pubs/acip-list.htm).

* Testing for HBsAg should not be performed within 30 days of receipt of hepatitis B vaccine.

**Because resolved past infection is uncommon in children, it may not be cost effective to test for anti-HBc and anti-HBs, particularly among children from low- or intermediate-endemicity areas (i.e., < 8%). In these cases, if the HBsAg is negative, children should be assumed to be nonimmune (susceptible) and should receive the full hepatitis B vaccine series according to Advisory Committee on Immunization Practices ACIP guidelines.

***Since many refugees will have received one or two doses of hepatitis B vaccine prior to departure, anti-HBs may be positive but not considered protective if the full series was not administered (Figure 1).

Hepatitis C

Adults

- At this time, routine screening for HCV (anti-hepatitis C antibody) infection for refugees during the new arrival medical examination* is not recommended unless they are members of high-risk groups, including:
    - Persons who ever injected illegal drugs
    - Persons with body art, including scars, tattoos, or body piercings
    - Persons with potential exposures to reused or nonsterile medical invasive devices
    - Persons who are HIV positive**
    - Persons who received whole blood or blood components prior to migration

- Persons with a history of multiple sex partners or of sexually transmitted infections
- Persons with other risk factors, such as chronic hemodialysis and other risk factors noted in the U.S. guidelines for medical screening (www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm)

Children <18 Years of Age

At this time, CDC does not recommend HCV screening for refugee children during the new arrival medical examination* unless they are members of high-risk groups, including:

- All children of hepatitis C virus-positive mothers
- All children who have ever injected illegal drugs
- All children with tattoos, body piercings, sexually active or history of abuse, or other exposures to reused or nonsterile invasive medical devices
- All children who are HIV positive**
- All children who received blood or blood components prior to migration

*Testing for HCV infection may be cost-effective in refugee populations from areas of high prevalence (e.g., rural Egypt, areas of Pakistan). If new refugee populations with known high prevalence rates begin to relocate to the United States, these guidelines will be revised with population-specific information.

**Immunocompromised persons, such as those infected with HIV, those who have end-stage renal disease, and those on immunosuppresant therapy, may have false-negative test results on antibody testing and should receive HCV RNA testing when indicated.

Hepatitis D

Routine screening for HDV infection is not recommended.

Acute Viral Hepatitis

Hepatitis A

Adults

Routine screening for hepatitis A virus infection is not recommended unless there is a clinical indication or unless vaccination is considered.

Children

Prevaccination screening for pre-existing immunity (total anti-HAV IgG) prior to vaccination in children may be cost-effective, depending on prevalence in the population and local medical costs.

Hepatitis E

Routine screening for hepatitis E virus infection is not recommended.

III. Discussion

A. Chronic Viral Hepatitis

1. Hepatitis B

Background Information on Hepatitis B Virus Infection

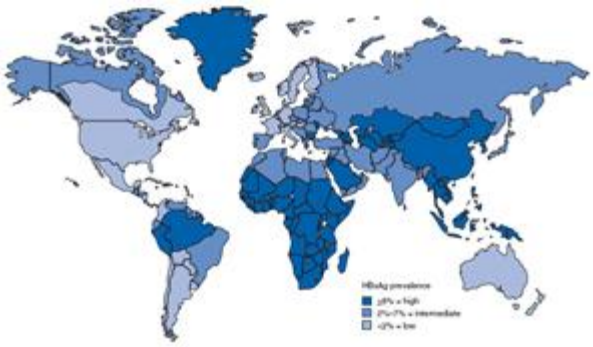

Figure 3. Geographic distribution of chronic hepatitis B virus (HBV) infection — worldwide, 2006*.

* For multiple countries, estimates of prevalence of hepatitis B surace antigen (HBsAg), a marker of chronic HBV infection, are based on limited data and might not reflect current prevalence in countries that have implemented childhood hepatitis B vaccination. In addition, HBsAg prevalence might vary within countries by subpopulation and locality.

Source: CDC. Traveler's health; yellow book. Atlanta, GA: US Department of Health and Human Services, CDC; 2008. Available at wwwn.cdc.gov/travel/yellowbookch4-HepB.aspx.

Chronic hepatitis B virus (HBV) infection is a major cause of preventable morbidity and mortality worldwide. Globally, more than 350 million people are chronically infected, leading to more than half a million deaths per year. The overwhelming majority of these deaths occur in resource-limited countries. Approximately 45% of the world's population lives in areas of high endemicity, where the prevalence of chronic HBV infection (i.e., hepatitis B surface antigen [HBsAg]) is >8%, and the lifetime risk of acquiring HBV infection is greater than 60% (Figure 3). Another 43% live in areas of intermediate endemicity, where the HBsAg prevalence is 2%-7%and the lifetime risk of infection is 20%-60%. The remaining 12% live in areas of low endemicity, where the HBsAg prevalence is <2% and the lifetime risk of infection is <20%. Most refugees arriving in the United States come from countries of intermediate and high HBV endemicity.

Persons with chronic HBV infection are at risk of developing HBV-related chronic liver disease, including cirrhosis and hepatocellular carcinoma, as well as extrahepatic manifestations (e.g., glomerulonephritis). Approximately 15%-25% of persons with chronic HBV infection will die prematurely from HBV-related cirrhosis or hepatocellular carcinoma.

Although usually asymptomatic, refugees with chronic HBV infection present an infection risk to others. Common modes of HBV transmission include perinatal and sexual transmission, needle sharing, and household exposure to persons with chronic infection. The virus is not known to be transmitted through breastfeeding.

Identification of infected persons during the new arrival refugee medical examination represents an opportunity to decrease morbidity and mortality in resettled refugees, as well as to prevent transmission to other family and close-contact community members. Although this document focuses on screening the newly arrived refugees, CDC has published recommendations for screening for chronic hepatitis B infection in the general U.S. population (www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm). The suggestions in this document are

consistent with these guidelines, and the reader is encouraged to review and be familiar with this broader document.

Epidemiology of HBV Infection in Refugees

HBV infection prevalence and transmission patterns vary markedly among different countries and between refugee populations. In general, prevalence rates of chronic HBV infection in migrant populations reflect the rates in the region of birth (Figure 3 and Table 1). Highly endemic regions (HBsAg ≥8%) include most of Asia, the Amazon Basin and parts of Latin America, the South Pacific Islands, and sub-Saharan Africa. Populations with the highest documented chronic HBV infection rates have originated in East Asia, Southeast Asia, and the Pacific (12%-18% in most studies). In these populations, the prevalence of anti-HBc among adults ranges from 63% to 93%. In highly endemic regions, most new infections occur among infants and young children and are the result of perinatal or horizontal household transmission. The sequelae of chronic HBV infection are largely related to the age of infection, and acquisition during infancy or childhood is particularly problematic; 25% of persons infected as infants and 15% of those infected at an older age die of cirrhosis, HCC or end-stage liver disease.

An additional 43% of the world's population resides in countries of intermediate HBV infection endemicity (HBsAg prevalence 2%-7%), which include countries in Asia, Africa, Eastern Europe, and some countries in South and Central America (Figure 3, Table 1). Countries of low endemicity (<2%, with the exception of indigenous populations) include the United States, Canada, Japan, Australia, New Zealand, and certain countries in Western Europe and in Central and South America.

Testing for HBV Infection

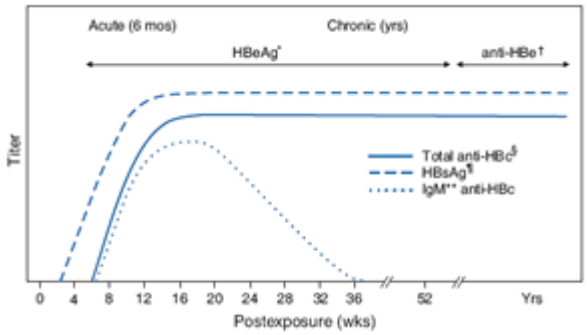

Figure 4. Typical serologic course of acute hepatitis B virus (HBV) infection with progression to chronic HBV infection.

The serologic patterns of HBV infection are complex, and a complete discussion is beyond the scope of this document. Briefly, antigens and antibodies associated with HBV infection include HBV surface antigen (HBsAg) and antibody to HBsAg (anti-HBs), HBV core antigen (HBcAg) and antibody to HBcAg (anti-HBc), HBV e-antigen (HBeAg) and antibody to HBeAg (anti-HBe). At least one serologic marker is present during each phase of HBV infection (Figure 4); however, the serologic markers most widely used in diagnosis of acute, resolving, and chronic HBV infection are HBsAg, anti-HBc and anti-HBs (Table 2).

A confirmed HBsAg-positive test result typically indicates HBV infection, and persons who have a positive HBsAg serologic test result should be considered infectious. Although HBsAg is

the first serologic marker to become positive after infection, the average time to detection after exposure is 30 days (range 10-60 days). Positive HBsAg has been reported in serum samples for up to 18 days following hepatitis B vaccination; however, this finding is of no clinical significance.[1],[2] In persons who recover from HBV infection, HBsAg and HBV DNA are eliminated from the blood while anti-HBs appears, typically within 3-4 months. In persons who become chronically infected, HBsAg and HBV DNA persist.

Anti-HBc appears at the onset of symptoms or when liver function test abnormalities appear in acute HBV infection; it persists for life. In certain persons, total anti-HBc is the only detectable HBV serologic marker. Isolated anti-HBc positivity can represent:

- resolved HBV infection in persons who have recovered but whose anti-HBs levels have waned, most commonly in high-prevalence populations;
- chronic infection in which circulating HBsAg is not detectable by commercial serologic assays, most commonly in high-prevalence populations and among persons with HIV or HCV infection (HBV DNA has been isolated from the blood in <5% of persons with isolated anti-HBc);
- false-positive reaction. In low-prevalence populations, isolated anti-HBc may be found in 10%-20% of persons with serologic markers of HBV infection, most of whom will demonstrate a primary response after hepatitis B vaccination. Persons positive only for anti-HBc are unlikely to be infectious except under unusual circumstances in which they are the source for direct percutaneous exposure of susceptible recipients to substantial quantities of virus (e.g., blood transfusion or organ transplant).

Acute HBV infection is marked by presence of the immunoglobulin M (IgM) class of anti-HBc, which may persist for up to 6 months after symptoms resolve.

Chronic HBV infection is confirmed by the absence of IgM anti-HBc in the setting of a positive HBsAg, or by the persistence of HBsAg for at least 6 months. Testing for serum IgM anti-HBc should be limited to persons with clinical evidence of acute hepatitis or an epidemiologic link to an identified case (Figure 4, Table 1).

Table 1. Typical interpretation of serologic test results for hepatitis B virus infection

Serologic marker				Interpreatation
HBsAg*	Total anti-HBc†	IgM§ anti-HBc	Anti-HBs¶	
-	-	-	-	Never infected and unimmunized
+	+	-	-	Chronic infection
-	+	-	+	Recovered from past infection and immune
+	+	+	-	Acute infection
-	-	-	+	Immune (vaccination ornatural) or false positive

* Hepatitis B surface antigen.
† Antibody to hepatitis B core antigen.
§ Immunoglobulin M.
¶ Antibody to HBsAg.

Table 2. Estimated number and precentage of hepatitis B surface antigen (HBs-Ag)-positive persons, by population segment — United States, 2006

Population segment	2006 population (millions)	HBsAg prevalence (%)	HBsAg-positive persons	
			No. (thousands)	(%)
U.S.-born, noninstitutionalized*	254.3	0.1	356	(30-50)
		(95% CI† = 0.1-0.2)	(229-534)	
Foreign-born§	37.5	1.0-2.6	375-975	(47-70)
Correctional instituitions¶	2.2	2.0	44	(3-5)
Other group living quarters**	6	0.5	30	(2-3)
Total	**300**	**0.3-0.5**	**805-1,405**	

* Source: 2006 American Community Survey, U.S. Census Bureau. Excludes persons living in correctional institutions and other group quarters. HBsAg prevalence estimates were derived from the National Health and Nutrition Examination Survey (CDC, unpublished data, 2008).
† Confidence interval.
§ Sources: 2006 American Community Survey, U.S. Census Bureau. Prevalence range represents estimates form the National Heatlh and Nutrition Examination Survey (1%) (CDC, unpublished data, 2008) and country-specific HBsAg estimates reported in the medical literature (2.6%) (CDC, unpublished data, 2008), applied to the estimated population by country of origin. Infant immunization programs in many countries have led to marked decreases in incidence and prevalence among younger, vaccinated members of these populations, which are largely not reflected in the medical literature (Wasley A, Kruszon-Moran D, Kuhnert W, et al. Hepatitis B prevalence in the U.S. in era of vaccination [Abstract 723], 45th Annual Meeting of the Infectious Diseases Society of America, San Diego, California; October 4-7, 2007).
¶ Sources: Sabol, W. J., T. D. Minton, and P. M. Harrison (2007, June). *Prison and Jail Inmates at Midyear 2006*. Revised March 12, 2008. NCJ 217675. Washington, DC: U.S. Department of Justice, Bureau of Justice Statistics. CDC, Prevention and control of Infectious with hepatitis viruses in correctional settings. MMWR 2003;52 (No. RR-1).
** Includes college dormitories, military quarters, nursing homes, group homes, and long-term care hospitals, as well as homeless persons. For persons in other group-living quarters, estimated

HBsAg prevalence was assumed to be equal to the mean prevalence in other groups. Source: 2006 American Community Survey, U.S. Census Bureau.

Recommendations for Testing for Chronic Hepatitis B Infection in Refugees

During the new arrival medical examination, screening for chronic HBV infection, including serologic assays for HBsAg, should be routinely performed on all refugees who are from or have resided in countries with intermediate (> 2%-7%) or high (≥8%) prevalence of chronic HBV infection (Figure 3, Table 1). Testing for anti-HBc and anti-HBs should also be considered, particularly if hepatitis B vaccine will be offered (Figure 1).

All HBsAg-positive persons should receive appropriate counseling and be evaluated for treatment. All persons living in households or other crowded living conditions with a chronically infected person should be tested for hepatitis B and, if susceptible and not infected, receive the 3-dose hepatitis B vaccine series.

Asymptomatic refugees who do not originate from or have not resided in countries where chronic HBV prevalence is either intermediate or high (≥2%) should undergo screening with serologic testing for HBsAg, anti-HBc and anti-HBs only if they are considered at increased risk according to CDC guidelines (www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm). Such persons include:

- Men who have sex with men (MSM)
- Persons with a history of injection drug use (IDUs)
- HIV-infected persons
- Persons with chronic liver disease (e.g., HCV-infected persons)
- Household contacts of persons with chronic HBV infection
- Persons from low-prevalence countries who are part of subpopulations that have known prevalence rates of 2% or greater (i.e., indigenous populations)
- Persons on hemodialysis therapy
- Persons with a history of multiple sex partners (> 1 more sex partners in six months) or a history of sexually transmitted infection
- Persons who have been employed in health-care settings or institutions where they cared for developmentally disabled persons
- Persons who have previously received whole blood or blood product transfusions
- History of incarceration, tattooing, body piercing, or exposure to unsterile medical devices.

In addition, any refugee who has had a potential exposure to HBV within 60 days of the new arrival examination should have repeat testing 3-6 months after arrival. This population should be advised to seek medical care if any hepatitis-related symptoms (e.g., jaundice, nausea/vomiting, right upper quadrant pain) occur during this period.

Special Considerations for Children and Pregnant Women

During the new arrival medical examination, screening for chronic HBV infection, using serologic assays for HBsAg, should be routinely performed on all refugees who are from or have resided in countries with intermediate (>2%-7%) or high (≥ 8%) prevalence of chronic HBV infection (Figures 2 and 3 and Table 1). In this case, if the HBsAg is negative, the child should be assumed to be nonimmune and should receive a full hepatitis B vaccine series. It is acceptable

to start the vaccine series while awaiting initial HBV serology results. Since the prevalence of resolved HBV infection is low in children, it may not be cost effective to test all children for anti-HBc--particularly in children from low or intermediate endemic areas (i.e., < 8%). However, any risk factor that increases pre-test probability for past or current HBV infection may be considered an indication for anti-HBc and anti-HBs testing. These risk factors include:

- Children with an immediate family member, particularly biological mother, who is chronically infected with HBV.
- Children from a low-prevalence country who are part of a subpopulation that has a known prevalence rate of ≥2% (e.g., some indigenous populations)
- HIV-infected children
- Children who received whole blood or blood components prior to migration.
- Children with a potential exposure to hepatitis B within 60 days of the new arrival examination should be tested again 3-6 months after arrival.
- Children with IDU or who have multiple sex partners or have a history of sexual exploitation.

In addition, any refugee child who had a potential exposure to hepatitis B within 60 days of the new arrival examination should have repeat testing 3-6 months after arrival. All children ≤18 years old who are HBsAg negative should receive the complete hepatitis B vaccination series according to the ACIP guidelines.

It is particularly important to screen pregnant women for HBsAg. Ninety percent of newborns born to a HBsAg-positive mother develop chronic infection and 25% die from cirrhosis, HCC or liver failure. Early identification of maternal infection can enable pre- and postnatal counseling and management to prevent transmission to the infant.

Vaccination Records

An increasing number of countries are including hepatitis B in their routine vaccination schedules. In addition, overseas initiation of the vaccine series for U.S.-bound refugees is increasing, particularly in populations originating in South and Southeast Asia. If a hepatitis B series has been initiated (and documented), it may be completed according to the Advisory Committee on Immunization Practices (ACIP) schedule. (www.cdc.gov/mmwr/preview/mmwrhtml/rr5416a1.htm?s_cid=rr5416a1_e and www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a1.htm?s_cid=rr5516a1_e) If the last recorded dose was given less than 30 days before the refugee screen, the HBsAg must be interpreted cautiously, since recent vaccination may result in a false-positive HBsAg. Likewise, antibody to hepatitis B surface Ag (anti-HBs) should not be checked in a person with an incomplete vaccine series, as a positive result in this situation does not assure immunity. For further discussion, see the immunization section of the domestic refugee medical screening guidelines (www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/immunizations-guidelines.html).

All refugees from intermediate (2%-7%) or high (≥ 8%) endemicity countries should have HBsAg testing, regardless of record of vaccination.

Clinical and Public Health Management of Persons with Chronic Hepatitis B Infection.

Persons with chronic HBV infection (HBsAg positive for at least six months) should be evaluated by a physician who is experienced and knowledgeable in the management of hepatitis B infection and liver disease. Certain patients with chronic HBV infection will benefit from treatment with antiviral therapy, while others must undergo routine and regular screening for disease progression. Clinicians who see a high volume of hepatitis B-infected patients may develop protocols to determine which patients will benefit most from referral to a specialist. Culturally sensitive patient education should be conducted, and materials provided in the refugee's primary language when possible (Box 1).

Persons who are HBsAg-positive are infected with HBV and should be considered infectious. Because hepatitis B is a reportable disease in some states, cases should be reported to the State or local health department, per state protocol.

Important Messages for Refugees Chronically Infected with Hepatitis B

Your test results show that you are infected with hepatitis B virus. This virus infects the liver:

- **General**
  - You may not feel ill with this disease, but you may need treatment and will need close monitoring for problems that it may cause in the future.
  - It is infectious and you can give it to others, especially if they have not been vaccinated for hepatitis B. Ways to prevent infecting someone else are listed below.
- **Prevention:**
  - All persons in your household and any persons in your community who you have close contact should be tested for hepatitis B.
  - All persons you have had sexual contact with should be tested for hepatitis B.
  - All close contacts, including sexual contacts, who are not infected with hepatitis B should and receive hepatitis B vaccination to protect them in the future.
  - The virus may be spread through sexual contact. You should notify your sexual partner(s) if you are infected and use methods, such as condoms, to help protect against spread.
  - Blood or body fluids can spread disease, so try not to expose others to your blood or body fluids:
    - Do not share household articles that might have your blood on them, such as toothbrushes, razors, or personal injection items such as insulin needles.
    - Cover cuts in your skin or other skin lesions.
    - Clean any spilled blood with a bleach solution.
  - If you are a pregnant woman, it is very important that your doctor or birth attendant is aware you are infected, so they can give your baby treatment that will prevent him or her from becoming infected.
  - This infection affects your liver, so you should avoid other things that can harm your liver:
    - Avoid alcohol

- Ask your doctor or pharmacist if medications you are taking might affect the liver. This includes medicines you might buy at the store without a prescription (especially acetaminophen, also known as Tylenol®)
- Ask your physician if you need vaccination against hepatitis A, another infection that can hurt your liver more, and if you need other protective vaccines (e.g., influenza or pneumococcal vaccines).
- Do not eat raw seafood, particularly oysters.

- Hepatitis B is not spread by breastfeeding, kissing, hugging, coughing, through food or water, sharing eating utensils or drinking glasses, or casual contact.

Involvement with a support group might help patients cope with chronic HBV infection. Information about support groups is available at www.hepprograms.org/support/hepb.asp and www.hepb.org/patients/support_groups.htm.

2. Hepatitis C

Background information on hepatitis C virus (HCV) infection

Figure 5. Geographic prevalence of hepatitis C virus infection.

Hepatitis C is a chronic, generally asymptomatic, form of viral hepatitis that can lead to cirrhosis and hepatocellular carcinoma (HCC). The prevalence of hepatitis C virus (HCV) varies between regions and countries (Figure 5), and an estimated 170 million people, or more than 3% of the world's population, are infected. HCV is transmitted through exposure to infected blood and/or other body fluids. In developed countries, infection primarily results from injection drug use. However, in developing countries, HCV is predominantly transmitted in medical settings where needles may be reused or through transfusions with infected blood products. Although transmission can occur through sexual contact, in the perinatal period, and through breastfeeding, these modes of transmission are inefficient and uncommon.

Most data on prevalence of HCV infection are derived from surveys of blood donors, outpatients, and other specific subpopulations that are not representative of the U.S.-bound refugee population. Prevalence is generally below 2% in the Americas, Europe, and Australia, while in most areas of Asia and Africa the rates exceed 2% (Figure 6). The highest recorded rates occur in Egypt (15% nationally and up to 30% in some villages), where HCV was iatrogenically spread during schistosomiasis control campaigns through use of contaminated parenteral needles.

Overall, 70% of HCV-infected persons will develop liver disease. Several factors may accelerate the progression of chronic hepatitis C, particularly moderate to high alcohol intake. Infection at

an older age is also associated with faster progression, as is co-infection with HIV. In Egypt, co-infection with schistosomiasis has been associated with more severe disease.

Epidemiology of HCV Infection in Refugee Populations

Little data are available on the epidemiology of HCV infection in refugee populations. Published prevalence rates of anti-HCV antibody have ranged from 0.1% of 1005 Kurdish refugees in Italy in 2003 to 8% of 234 Cambodian refugees in Australia in 2005.[3] One of the larger reports from Canada, involving more than 22,000 asylum seekers, found an HCV infection rate of 1.5%.4 This was a particularly strong study since cases were confirmed by detection of RNA by PCR, eliminating the chance of false-positive results. Asylum seekers in Italy were reported to have rates of 4.5% in another study.[5] No published prevalence data are available for refugees arriving in the United States. Unpublished data from the Minnesota refugee health database indicated that of more than 20,000 new arrivals during 2004–2010, 694 were tested for HCV infection. Of these, 26 (3.7%) had antibody against HCV detected (personal communication, Blain Mamo). This number is likely an overestimate, as many of these persons may have been tested due to the presence of risk factors for (e.g., tattoos) or signs/symptoms (e.g., elevated liver enzymes) of HCV infection.

Recommendations for Testing of Refugees for Chronic HCV Infection

CDC does not recommend routine screening of refugees arriving in the United States for HCV infection. Sroczynski et al. recently suggested that screening populations who have a prevalence of <10% is not cost-effective due to many factors; high rates of false-positive screening tests, relatively poor efficacy of treatment, the high adverse-event profile of treatment medications, and the low number of people who are eligible for treatment due to co-morbidities such as substance abuse, psychiatric illness of medical diseases (37%).[6] However, a recent Canadian study of immigrants with chronic HCV demonstrated that immigrant populations (including both refugees and other immigrants) were less likely than the general population of Canada to have a history of intravenous drug use as a contraindication (20% vs. 67%).[7] This study has led some authors to suggest a > 3% baseline prevalence rate as a threshold for testing in immigrant and refugee populations.[8] At this time, refugee populations arriving in the United States have not had high rates of hepatitis C documented. CDC will issue population-specific guidance when/if it is determined that certain populations are at an increased risk and routine screening would be warranted. Clinicians and state programs are always encouraged to notify CDC's Division of Global Migration and Quarantine when any new or increased-prevalence infections or diseases of concern are observed in refugee populations (e-mail: cdcinfo@cdc.gov).

Risk factors identified through epidemiologic studies in other populations can be assumed to confer increased risk to refugees. Therefore, refugees with risk factors for hepatitis C should be screened with anti-HCV antibody. The most common risk factors encountered in this population include:

- HIV infection
- History of tattooing, body piercing, or other known exposures to nonsterile or reused medical devices
- History of having received blood or blood components,
- History of multiple sex partners or sexually transmitted diseases.

In addition, all biological infants and children of HCV-infected mothers should be tested. Other risk factors may be indications for HCV screening, and the reader is encouraged to review the U.S. recommendations for hepatitis C testing and management (www.cdc.gov/hepatitis/HCV/Management.htm).

Other risk factors in refugee populations may not have been identified, such as female genital cutting with contaminated instruments. Further investigation of prevalence rates and risk factors for infection are encouraged in refugee populations.

A positive anti-HCV antibody test result must be interpreted in context of both the pre-test probability and the natural history of HCV infection*: A positive anti-HCV by ELISA has a positive predictive value of greater than 95% when it is used in patients with a high risk of HCV infection (e.g., in the United States, those with a history of intravenous drug use or abnormal liver chemistry findings). However, the positive predictive value is only 50%-60% in patients at low risk for HCV infection. In addition, approximately 15% of persons will clear the infection but continue to test positive for anti-HCV antibodies.

Testing of low-risk populations is discouraged; such testing increases the likelihood of both false-positive and false-negative results. Further research defining the actual HCV infection rates of subpopulations of refugees is needed and should be encouraged, since such studies can help target screening efforts.

*Immunocompromised persons, such as those infected with HIV, those who have end-stage renal disease, and those on immunosuppresive therapy, may have false-negative tests and should receive HCV RNA testing when indicated.

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Persons who have a positive anti-HCV antibody test should receive confirmatory RNA testing by PCR. Those who are confirmed to have HCV infection should be referred for consultation to a physician experienced and knowledgeable in the management of chronic liver disease and hepatitis C. Certain patients with chronic HCV infection (particularly with specific genotypes) will benefit from treatment with antiviral therapy. Culturally sensitive patient education should be conducted, and materials should be provided in the refugee's primary language when possible.

3. Hepatitis D

Hepatitis D virus (HDV) is a defective virus that requires the presence of HBV to be viable in the human host. It may be acquired as a co-infection with HBV or as a superinfection after hepatitis B infection. An estimated 5% of the world's 300 million chronic HBV-infected persons are co-infected with HDV. Chronic HBV carriers who are superinfected with HDV usually also develop chronic HDV infection. Progression to cirrhosis and HCC is believed to be more common with HBV/HDV co-infections than with HBV infection alone. Identified risk groups include

- Men who have sex with men
- Hemodialysis patients
- Persons with infected sexual contacts
- Injection drug users
- Health care and public safety workers
- Infants born to infected mothers (extremely rare).

The epidemiology of chronic HDV infection in refugees is unknown.

Since HDV cannot infect in the absence of HBV infection, hepatitis B vaccination is a primary preventive measure for HDV infection. Chronically infected persons may be treated with the same antiviral agents that are used to treat the primary hepatitis B infection.

Recommendations for testing of refugees for HDV infection

CDC does not recommend routine testing for HDV infection in refugees arriving in the United States.

B. Acute Viral Hepatitis

1. Hepatitis A

Figure 6. Estimated prevalence of hepatitis A virus, 2005

Hepatitis A virus (HAV) is the most common etiology of acute hepatitis. It is endemic worldwide (Figure 6). Most refugees resettling to the United States are from areas that are highly endemic for HAV. HAV is transmitted via the fecal-oral route, and infection is associated with poor sanitation and hygiene. In highly endemic areas, most persons are infected as children. Most refugees resettling to the United States, especially adults, are immune to HAV infection due to previous exposure; resolved HAV infection results in lifetime immunity and does not lead to chronic infection.

Recommendations for testing of refugees for HAV infection

Routine testing for HAV infection is not recommended at any age. Individuals with signs or symptoms of acute HAV infection (e.g., jaundice, abdominal pain, vomiting, elevated liver enzymes) should be evaluated for active HAV infection (anti-HAV IgM).

Some young children may be asymptomatic but infected with HAV at the time of migration to the United States. The risk of spread to the general population from these children is unknown. Outbreaks have been associated with asymptomatic internationally adopted children placed in nonimmune populations (e.g., host families, day care). Because refugees, unlike international adoptees, tend to group together following migration (at least initially), and since refugee populations are likely generally immune to HAV infection, the potential for an outbreak among resettled refugees is limited. Screening for active asymptomatic infection in children is expensive and demands extensive public health intervention when detected. Therefore, CDC does not recommend routine testing for acute hepatitis A in asymptomatic refugees.

Ideally, hepatitis A vaccine (at least the initial dose) should be administered to refugees prior to migration to the United States to decrease the risk of viral shedding by infected but asymptomatic individuals. Young children, who may shed virus for several months following an asymptomatic HAV infection, are of particular concern However, refugees currently do not receive pre-departure hepatitis A vaccination.

In the United States, hepatitis A vaccine is recommended for all children 1-18 years of age. Pre-vaccine testing for Hepatitis A antibody (total anti-HAV IgG) may be considered for refugee children resettling in the United States. The age limit above which it is less cost-effective to conduct pre-vaccine serologic screening is unknown but clearly depends on the prevalence of HAV infection in the specific population. For more information on HAV vaccine recommendations, see the immunization guidelines section for newly arrived refugees (www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/domestic-guidelines.html) and the ACIP guidelines for the United States (www.cdc.gov/vaccines/pubs/acip-list.htm).

2. Hepatitis E

Hepatitis E virus (HEV) causes acute viral hepatitis that is transmitted by the fecal-oral route. The signs and symptoms are similar to those produced by HAV. HEV infection is well described in many resource-limited nations, particularly those in South Asia, although its prevalence is likely underestimated, including in the developed nations.[9] Although fulminant hepatitis may develop in 0.5%-4 % of the overall HEV-infected population, it is particularly virulent in pregnant women, especially those infected during their third trimester, when mortality rates of up to 25% have been reported. The incubation period of HEV ranges from 3 to 8 weeks, with a mean of 40 days. Chronic infection has not been reported among otherwise healthy persons. Only persons with signs or symptoms of acute hepatitis should be tested for HEV infection--along with HAV, HBV, and HCV infection, since these hepatitides are clinically indistinguishable. The diagnosis is confirmed by detection of RNA in the blood by reverse transcriptase-polymerase chain reaction. Recent reports suggest that the rates of acute HEV infection are increasing and may be chronic among HIV-positive patients.[10]

Recommendations for testing of refugees for HEV infection

Currently, CDC does not recommend routine screening of refugees for HEV infection.

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